

**WORLD INTELLECTUAL PROPERTY ORGANIZATION
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY
EUROPEAN PATENT OFFICE**

Docket No.: 03260.0093-00304 (2517-WO)

Date: 13 February 2001

In the Application of: Immunex Corporation
Int'l. Application No.: **PCT/US00/01338**
Int'l. Filing Date: 21 January 2000
For: METALLOPROTEINASE-DISINTEGRIN FAMILY MEMBERS:
SVPH DNAS AND POLYPEPTIDES

RESPONSE TO WRITTEN OPINION

European Patent Office
D-80298 Munich
GERMANY

Attn: K. Giebeler, Authorized Officer / Examiner

In response to the Written Opinion mailed 13 November 2000, and further to Applicant's Request for Extension of Time Under PCT Rule 66.2(d) dated 12 February 2001, Applicants request that the claims be amended under PCT Article 34 in accordance with the accompanying replacements for pages 71-74 of the PCT application. The replacement sheets include amendments to claims 1-2, 5, 9-10, 13, 15, 23-24, and 27 and the addition of new claims 43-44.

The Examiner is requested to note that an attorney for Applicant submitted to the International Bureau a Power of Attorney naming her as agent for Applicant and an Amendment under Article 19 and Rule 46. However, according to Rule 66.1(c), any such Article 19 amendments are superseded by the present amendments under Article 34, and the Examiner may disregard the Article 19 Amendment should it be received by the IPEA.

Claims 1-2, 5, 9-10, 13, 15, 23-24, and 27 have been amended and new claims 43-44 have been added in a manner as set forth below, with the original text of the claim that is to be deleted by the present Amendment enclosed within brackets, and the text that has been added by the present Amendment in bold. Claims 1-2, 5, and 13 have been amended to include the following language:

disintegrin, polypeptides, and particular regions of the amino acid sequences of SEQ ID NOS 12-14. Claims 15 and 27 have been amended to add claim language pertaining to

particular regions of the amino acid sequences of SEQ ID NOs 15-16. Claims 1 and 15 have been amended to specify a minimum length for nucleic acids that hybridize, and to move subparagraphs (d) and (f) to new claims 43 and 44. Claims 9-10 and 23-24 have been amended to simplify the language of the claims. Claims 10 and 24 have been amended to change the recitations of SVPH 1 or 4 polypeptides to polypeptides according to claim 4 or 18, respectively. The amendments are believed to be fully supported by the specification. In particular, the amendments to claims 1 and 13 relating to SEQ ID NOs 12-14 are supported by the disclosure at page 23, lines 8-17; the amendments to claims 15 and 27 relating to SEQ ID NOs 15-16 are supported by the disclosure at page 23, lines 18-26, and the amendments to claims 1 and 15 relating to lengths of nucleic acids that hybridize are supported by the disclosure at page 45, lines 10-13.

1. An isolated SVPH nucleic acid molecule selected from the group consisting of:

(a) an isolated nucleic acid molecule comprising a [the] DNA sequence selected from the group consisting of [SEQ ID NO:1,] SEQ ID NO:7, SEQ ID NO:8, and SEQ ID NO:9;

(b) an isolated nucleic acid molecule encoding an amino acid sequence comprising the sequence selected from the group consisting of [SEQ ID NO:4,] SEQ ID NO:12, SEQ ID NO:13, and SEQ ID NO:14;

(c) an isolated nucleic acid molecule encoding an amino acid sequence comprising a sequence selected from the group consisting of amino acids 1 through 15 of SEQ ID NO:12, amino acids 16 through 188 of SEQ ID NO:12, amino acids 189 through 388 of SEQ ID NO:12, amino acids 389 through 491 of SEQ ID NO:12, amino acids 492 through 675 of SEQ ID NO:12, amino acids 676 through 698 of SEQ ID NO:12, amino acids 699 through 766 of SEQ ID NO:12, amino acids 699 through 787 of SEQ ID NO:13, and amino acids 699 through 820 of SEQ ID NO:14;

[(c)] (d) an isolated nucleic acid molecule that comprises at least about 17 contiguous nucleotides and that hybridizes to either strand of a denatured, double-stranded DNA comprising [the] a nucleic acid sequence of [(a) or (b)] (c) under conditions of moderate stringency in 50% formamide and 6XSSC, at 42°C with washing conditions of 60°C, 0.5XSSC, 0.1% SDS; and

(e) an isolated nucleic acid molecule degenerates from [SEQ ID NO:1,] SEQ ID NO:7, SEQ ID NO:8, and SEQ ID NO:9 as a result of the genetic code]; and

[(f) an isolated nucleic acid molecule selected from the group consisting of human SVPH 1 DNA; an allelic variant of human SVPH 1 DNA; and a species homolog of SVPH 1 DNA].

2. The nucleic acid molecule of claim 1 selected from the group consisting of [SEQ ID NO:1,] SEQ ID NO:7, SEQ ID NO:8, and SEQ ID NO:9.

5. An isolated polypeptide according to claim 4 having a molecular weight selected from the group consisting of approximately [4,199;] 86,983; 89,459; and 92,781 Daltons as determined by SDS-PAGE.

9. A host cell [transfected or transduced with] comprising the vector of claim 3.

10. A method for the production of [SVPH 1] a polypeptide according to claim 4 comprising culturing a host cell of claim 9 under conditions promoting expression[, and recovering the polypeptide from the culture medium].

13. An isolated metalloproteinase-disintegrin polypeptide comprising an amino acid sequence selected from the group consisting of [SEQ ID NO:4,] SEQ ID NO:12, SEQ ID NO:13, [and] SEQ ID NO:14, amino acids 1 through 15 of SEQ ID NO:12, amino acids 16 through 188 of SEQ ID NO:12, amino acids 189 through 388 of SEQ ID NO:12, amino acids 389 through 491 of SEQ ID NO:12, amino acids 492 through 675 of SEQ ID NO:12, amino acids 676 through 698 of SEQ ID NO:12, amino acids 699 through 766 of SEQ ID NO:12, amino acids 699 through 787 of SEQ ID NO:13, and amino acids 699 through 820 of SEQ ID NO:14.

15. An isolated SVPH nucleic acid molecule selected from the group consisting of:

(a) an isolated nucleic acid molecule comprising a [the] DNA sequence selected from the group consisting of SEQ ID NO:3, SEQ ID NO:10, and SEQ ID NO:11;

(b) an isolated nucleic acid molecule encoding an amino acid sequence comprising the sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:15, [and] SEQ ID NO:16[:], amino acids 686 through 713 of SEQ ID NO:15, amino

comprising a sequence selected from the group consisting of amino acid 1 through 27 of SEQ ID NO:15, amino acids 28 through 193 of SEQ ID NO:15, amino acids 194 through

392 of SEQ ID NO:15, amino acids 393 through 493 of SEQ ID NO:15, amino acids 494 through 685 of SEQ ID NO:15;

[(c)] (d) an isolated nucleic acid molecule that comprises at least about 17 contiguous nucleotides and that hybridizes to either strand of a denatured, double-stranded DNA comprising [the] a nucleic acid sequence of [(a) or (b)] (c) under conditions of moderate stringency in 50% formamide and 6XSSC, at 42°C with washing conditions of 60°C, 0.5XSSC, 0.1% SDS; and

[(d) an isolated nucleic acid molecule derived by *in vitro* mutagenesis from SEQ ID NO:3, SEQ ID NO:10, and SEQ ID NO:11;]

(e) an isolated nucleic acid molecule degenerate from SEQ ID NO:3, SEQ ID NO:10, and SEQ ID NO:11 as a result of the genetic code[; and]

[(f) an isolated nucleic acid molecule selected from the group consisting of human SVPH 4 DNA; an allelic variant of human SVPH 4 DNA; and a species homolog of SVPH 4 DNA].

23. A host cell [transfected or transduced with] comprising the vector of claim 17.

24. A method for the production of [SVPH 4] a polypeptide according to claim 18 comprising culturing a host cell of claim 23 under conditions promoting expression[, and recovering the polypeptide from the culture medium].

27. An isolated metalloproteinase-disintegrin polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:15, [and] SEQ ID NO:16, amino acids 1 through 27 of SEQ ID NO:15, amino acids 28 through 193 of SEQ ID NO:15, amino acids 194 through 392 of SEQ ID NO:15, amino acids 393 through 493 of SEQ ID NO:15, amino acids 494 through 685 of SEQ ID NO:15, amino acids 686 through 713 of SEQ ID NO:15, amino acids 714 through 790 of SEQ ID NO:15, and amino acids 714 through 781 of SEQ ID NO:16.

43. The nucleic acid molecule of claim 1 selected from the group consisting of (a) an isolated nucleic acid molecule derived by *in vitro* mutagenesis from SEQ ID NO:7, SEQ ID NO:8, and SEQ ID NO:9; and

(b) an isolated nucleic acid molecule selected from the group consisting of

44. The nucleic acid molecule of claim 15 selected from the group consisting